REMARKS

Claims 1-29 are pending. Claims 1-9, 12-23, and 25-27 are rejected. Claim 15 is objected to because of informalities. Claims 10, 11, and 24 are objected to but the Examiner states would be allowable if rewritten in independent form to include the limitations of the base claim and any intervening claims. Claims 28 and 29 are added. Claim 15 is presently amended. As a result of this amendment and the discussion below, it is believed that all claims are patentable and that this application is now in condition for allowance.

Summary of the Invention of the Present Application:

The invention of the present application provides a composition and method for determining compliance with a medication regimen. This composition and method is rapid, simple, and inexpensive. In one embodiment, it includes an orally administrable composition in combination with at least one visual marker. This marker is present in a form and amount sufficient to cause a coloration of at least a portion of a mucous membrane or buccal membrane of the oral and/or pharyngeal cavity of a patient. In various embodiments of the invention, by way of non-invasive observation of this coloration of the mucous or buccal membrane of the oral and/or pharyngeal cavity, one may obtain information regarding patient compliance with a medication regimen, such as whether the medication has been taken, the time elapsed since the medication was last taken, whether it is time for another dose of medication, etc. Thus, the present

invention is very rapid, simple, and non-invasive as opposed to more invasive, tedious, and complicated monitoring methods of the prior art, such as the analysis of urine and stool samples, and injection of compositions.

Claim Objections:

The Examiner has objected to claim 15, stating that the claim recitation "said subject"at line 6 should be "said patient." Claim 15 has been presently amended to correct this minor typographical error.

Claim Rejections 35 U.S.C. § 102:

The Examiner has rejected claims 15-20 and 22 under 35 U.S.C. § 102(b) as being anticipated by Singh (U.S. Patent No. 5,458,879). In particular, regarding claim 15, the Examiner states that Singh discloses an oral composition containing a coloring agent or marker wherein the composition coats and adheres to the throat and mucous membranes, and that visible coloration of the mucous membranes is an inherent property of the coloring agent. Applicants respectfully disagree.

Applicants note that Singh is directed to an aqueous oral composition including a mucoadhesive. The mucoadhesive is used to retain a medicament, such as an antitussive, in the throat for longer periods in order to enhance its effectiveness. Applicants further note that while Singh does mention colorants as an optional ingredient (including FD&C Red No. 40) in an oral composition, such colorants find their use solely for the purpose of imparting a particular color to the composition of Singh.

They have no purpose and indeed teach no purpose beyond that. In other words, the colorants are used to provide an aesthetic, cosmetic characteristic (color) to the composition, much like a flavoring agent would be used to make the composition more palatable. In fact, at column 7, lines 45-46, Singh states that the purpose of the colorants is to produce a "pleasant looking final product." There is no teaching in Singh that such colorants function as anything but as a superficial component for aesthetic and cosmetic purposes. That is, they are essentially "throw-away" components with respect to the therapeutic action provided by the composition. They certainly do not teach the invention utilizing a marker in a form and sufficient amount to cause coloration of a patient cavity for subsequent visual observation to determine compliance with a medication regimen.

Applicants submit that the use of colorants as "throw-away" components in Singh is very apparent when one considers the disclosure of column 7, lines 42-47. The paragraph includes a mere list of ingredients which may be included in the composition. These ingredients may include "natural or artificial sweeteners, flavoring agents, colorants and the like." The subsequent Examples go on to simply list "colorants," including "FD&C Red # 40." However, there is no indication that the colorant plays any significant role in the composition of Singh, nor does Singh teach that the colorant is present in a form and amount sufficient to stain the oral and/or pharyngeal cavity for subsequent visual observation to determine compliance with a

medication regimen. In contrast, the marker of the composition of the present application is what allows an observer to determine compliance, duration since last medication, remaining time until next medication, etc. There simply is no teaching in Singh by which one of skill in the art may use the composition disclosed therein to obtain such information.

Further, as mentioned above, Applicants assert that there is absolutely no teaching in Singh that the colorant is provided in a form and sufficient amount to cause coloration of a part of the oral and/or pharyngeal cavity such that it is used as a marker to determine whether a patient has complied with a medication regimen, as is recited in the claims of the present application. First, Applicants submit that the composition of Singh is taught as having a wholly different purpose than that of the present application. Reference to the entirety of Singh makes it quite clear that the purpose of the composition of that reference lies in that it includes a mucoadhesive to promote retention of a medicament, such as an antitussive, in the oral and/or pharyngeal cavity. Nowhere does Singh discuss or teach that the colorant actually marks the adhesive and can be seen. Rather, as described above, the colorant of Singh is merely used to impart an aesthetic, cosmetic quality to the composition. Second, Applicants submit that the amount of colorant in the Singh composition, while providing color to the composition, does not provide an amount sufficient to cause significant coloration such that it is visually observable after ingestion to determine compliance, and other issues,

such as the duration since the last medication. In Singh, the amount of coloring agent in the composition is recited in the Examples as between .005 and .030 weight percent of the total composition. Applicants assert that this is not a sufficient amount to cause an observable coloration in a patient in order to determine compliance. Any instantaneous, minor coloring presented immediately after the Singh composition is consumed would be so short-lasting or fleeting that to even be possibly observed, it would have to be done so immediately. That is, the observer might as well be present to dispense the medication. As may be appreciated, this defeats the entire purpose of the invention. Therefore, Singh does not in any way teach or suggest the invention as claimed nor would it be usable for the invention.

Further, nowhere does Singh teach that the coloring agent would be visually observable in that such observation would require a second person to check for compliance. Were a second person to observe a patient ingesting the composition, then there would be no need to observe the oral and/or pharyngeal cavity. Singh does not affirmatively teach any such observation of the oral and/or pharyngeal cavity. And since the amount of colorant in Singh is not sufficient to cause an observable coloration, such observation cannot be inherent in Singh, either.

In view of the above, Applicants respectfully request a withdrawal of the rejection of claims 15-20, and 22 under 35 U.S.C. § 102(b).

Claim Rejections 35 U.S.C. § 103:

1. **Rittenburg/Singh**

The Examiner has rejected claims 1-9 under 35 U.S.C. § 103(a) as being unpatentable over Rittenburg (U.S. Patent No. 6,068,981) in view of Singh. In particular, the Examiner states that Rittenburg discloses oral administration of a composition including a marker that passes into a tissue and can be detected. The Examiner further states that coloration of tissues is a function of this composition, and thus coloration of the oral and/or pharyngeal cavity would result if the composition of Singh were to be ingested. Applicants respectfully disagree.

Claim 1 recites that contact coloration occurs in a mucous or buccal membrane of the oral and/or pharyngeal cavity. Applicants submit that Rittenburg does not teach contact coloration of the mucous or buccal membrane of the oral and/or pharyngeal cavity, as claimed in the present application. Rather, Applicants submit that the colorimetric analyses described in Rittenburg involve an analysis for color in a sample, such as urine, taken from the subject (for example, see column 11, line 49 to column 12, line 7). Further, Rittenburg does not disclose visualization of the oral and/or pharyngeal cavity to determine compliance with a medication regimen, as is recited in claim 1. Rather, Applicants submit that Rittenburg discloses a compound that passes into a system (such as bloodstream, excretory, or other fluid or tissue), and then detects a marker in a fluid or tissue sample taken from the subject (see at least column 2, lines

61-62; column 3, lines 6-7 and 42-43; and column 4, lines 2-3, 13-14, 31-34, and 53). These methods described in Rittenburg are very invasive and time consuming. And, these are the very drawbacks with previous marking methods that were discussed in the "Background of the Invention" section of the present application, and which the invention of the present application overcomes.

Applicants further submit that Singh does not cure the defects of the Rittenburg reference, because Singh does not provide any of the elements of claim 1 that are missing from Rittenburg. Singh does not disclose visually observing the oral and/or pharyngeal cavity of a patient. And, as described above, Singh does not teach contact coloration to be observed to determine compliance. In Singh, the amount of coloring agent in the composition is recited in the Examples as between .005 and .030 weight percent of the total composition. Applicants assert that this is not a sufficient amount to cause an observable coloration in a patient in order to determine compliance. As described above, any instantaneous, minor coloring presented immediately after the Singh composition is consumed would be so short-lasting or fleeting that to even be possibly observed, it would have to be done so immediately, which defeats the entire purpose of the invention.

Thus, neither Rittenburg nor Singh teaches visualization of the oral and/or pharyngeal cavity; neither does either of the references teach a marker in an amount to cause contact coloration of oral and/or pharyngeal membranes to determine

compliance. As such, any combination of Rittenburg and Singh does not teach every limitation of claim 1, and thus cannot render claim 1 obvious. Further, since Rittenburg and Singh (and the colorants thereof) are directed to different compounds with different uses for different purposes, there would be no motivation for one skilled in the art to combine the two references. Therefore, Applicants respectfully request a withdrawal of the rejection of independent claim 1, and dependent claims 2-9.

2. **Rittenburg/Blase**

The Examiner has rejected claims 12-14 under 35 U.S.C. § 103(a) as being unpatentable over Rittenburg in view of Blase (U.S. Patent No. 5,272,137). In particular, the Examiner states that Rittenburg discloses oral administration of a composition including a marker that passes into a tissue and can be detected. The Examiner further states that coloration of tissues is a function of this composition, and thus contact coloration of the oral and/or pharyngeal cavity would result if the composition with multiple dyes or markers of Blase were to be ingested. Applicants respectfully disagree.

Each of claims 12-14 depends from claim 1 and thus incorporate the limitations of claim 1. As described above, claim 1 is not rendered obvious by the combination of Rittenburg and Singh. Thus, for any of claims 12-14 to be rendered obvious by the combination of Rittenburg and Blase, claim 1 must either (1) be

anticipated by Rittenburg or Blase, or (2) be obvious in view of the combination of Rittenburg and Blase. Applicants assert that neither is the case.

As described above, Rittenburg does not teach contact coloration of the mucous or buccal membrane of the oral and/or pharyngeal cavity, as is recited in claim 1. Further, Rittenburg does not disclose visualization of the oral and/or pharyngeal cavity to determine compliance with a medication regimen, as is recited in claim 1. Rather, Rittenburg discloses a compound that passes into a system (such as bloodstream, excretory, or other fluid or tissue), and then detects a marker in a fluid or tissue sample taken from the subject. The methods of Rittenburg are thus very invasive and time consuming. These are the very drawbacks with previous marking methods that were discussed in the "Background of the Invention" section of the present application, and which the invention of the present application overcomes.

Applicants further submit that Blase does not cure the defects of the Rittenburg reference, because Blase does not provide any of the elements of claim 1 that are missing from Rittenburg. Blase does not disclose visually observing the oral and/or pharyngeal cavity of a patient. And, Blase does not teach contact coloration to be observed to determine compliance.

Blase is directed to a pharmaceutical suspension composition including a stabilizing effective amount of xanthan gum and microcrystalline cellulose. The composition of Blase also includes various flavoring agents. The purpose of Blase then

is to provide a suspension that minimizes sedimentation of active pharmaceutical ingredients and provides a pleasant-tasting liquid dosage. Applicants note that this is wholly unrelated to the subject matter of the present application. Applicants further note that while Blase does list various coloring agents, including FD&C Red No. 40, FD&C Blue No. 1, and FD&C Red No. 33 in an oral composition, such coloring agents find their use solely for the purpose of imparting a particular color to the composition of Blase. They have no purpose and indeed teach no purpose beyond that. In other words, like the colorants of Singh, the coloring agents of Blase are used to provide an aesthetic, cosmetic characteristic (color) to the composition, much like a flavoring agent would be used to make the composition more palatable. In fact, at column 6, lines 3-4, Blase states that the purpose of the coloring agents is "to provide an appealing color to the suspension." There is no teaching in Blase that such coloring agents function as anything but as a superficial component for aesthetic and cosmetic purposes. Again, these are essentially "throw-away" components with respect to the therapeutic action provided by the composition. They certainly do not teach the invention utilizing a marker in a form and sufficient amount to cause coloration of a patient cavity for subsequent visual observation.

Applicants submit that the use of coloring agents as "throw-away" components in Blase is very apparent when one considers the disclosure of column 3, lines 56-60. The paragraph includes a mere list of ingredients which may be included in

the composition. These ingredients are described as "additives," and may include "wetting agents, defoaming agents, surfactants, buffers, electrolytes, ...preservatives, colorings, flavorings, sweeteners, and sequestering agents." The subsequent paragraphs go on to simply list examples of these additives, including coloring agents. However, there is no indication that the coloring agent plays any significant role in the composition of Blase, nor does Blase teach that the coloring agent is present in a form and amount sufficient to stain the oral and/or pharyngeal cavity for subsequent visual observation to determine compliance with a medication regimen. In contrast, the coloring agent of the composition of the present application is what allows an observer to determine compliance, duration since last medication, remaining time until next medication, etc. There simply is no teaching in Blase by which one of skill in the art may use the composition disclosed therein to obtain such information.

Also, the Examiner cites Blase for its disclosure of multiple dyes (being multiple markers). Applicants disagree. The purpose of using multiple dyes in one composition in Blase is to mix two colors to produce a third color for the suspension (see column 10, lines 6-9, discussing the mixing of blue and red coloring agents to provide a purple color to the composition). This in no way discloses multiple markers as described in the present application (for example, see p. 17, lines 6-16 of the application, disclosing a composition including a first marker detectable under natural

light and a second marker detectable only under light that causes fluorescence, wherein each marker has a different duration).

Further, even in Blase disclosed multiple markers in a composition (which it does not), Applicants still assert that there is absolutely no teaching in Blase that the coloring agent is provided in a form and sufficient amount to cause coloration of a part of the oral and/or pharyngeal cavity such that it is used as a marker to determine whether a patient has complied with a medication regimen, as is recited in the claims of the present application. First, the composition of Blase is taught as having a wholly different purpose than that of the present application. Reference to the entirety of Blase makes it quite clear that the purpose of the composition of that reference lies in that it includes a stabilizing effective amount of xanthan gum and microcrystalline cellulose to form a suspension. Nowhere does Blase discuss or teach that the use of the coloring agent is part of a method for monitoring patient compliance. Rather, as described above, the coloring agent of Blase is merely used to impart an aesthetic, cosmetic quality to the composition. Second, the amount of coloring agent in the Blase composition, while providing color to the tablet, does not provide an amount sufficient to cause significant coloring such that it is visually observable after ingestion to determine compliance, and other issues, such as the duration since the last medication. In Blase, the amount of coloring agent in the composition is recited in Table 1 and in the Examples as between .0005 and .003 g per 100 ml of the composition in suspension

form. Applicants assert that this is not a sufficient amount to cause an observable coloration in a patient in order to determine compliance. Any instantaneous, minor coloring presented immediately after the Blase composition is consumed would be so short-lasting or fleeting that to even be possibly observed, it would have to be done so immediately. That is, the observer might as well be present to dispense the medication. Like Singh, as may be appreciated, this defeats the entire purpose of the invention.

Thus, neither Rittenburg nor Blase teaches visualization of the oral and/or pharyngeal cavity, nor does either of the references teach a marker in an amount to cause contact coloration of the oral and/or pharyngeal membranes to determine compliance. As such, any combination of Rittenburg and Blase does not teach every limitation of claim 1, and thus cannot render claim 1 obvious. Therefore, as claim 1 is not rendered obvious, dependent claims 12-14 are also not obvious. Further, neither of the references teaches multiple markers as disclosed in the present application. Further, since Rittenburg and Blase (and the colorants thereof) are directed to different compounds with different uses for different purposes, there would be no motivation for one skilled in the art to combine the two references. Thus, Applicants respectfully request a withdrawal of the rejection of claims 12-14.

3. **Singh/Pather**

The Examiner has rejected claim 21 under 35 U.S.C. § 103(a) as being unpatentable over Singh in view of Pather (U.S. Patent No. 6,200,604). The Examiner

states that Singh does not teach carmine red but that Pather does teach its use. Applicants respectfully disagree that claim 21 is obvious over Singh in view of Pather.

Claim 1 depends from claim 15 and thus incorporates the limitations of claim 15. As described above, claim 15 is not anticipated by Singh. Thus, for claim 21 to be rendered obvious by the combination of Singh and Pather, claim 15 must either (1) be anticipated by Pather, or (2) be obvious in view of Singh and Pather. However, Applicants assert that neither Singh nor Pather teaches a coloring agent provided in an amount to cause coloration of the oral and/or pharyngeal cavity to determine compliance with a medication regimen. Thus, neither Singh nor Pather, alone or in combination, can anticipate or render obvious claim 15. And thus, the combination of Singh and Pather cannot render claim 21 obvious.

As described above, Applicants assert that there is absolutely no teaching in Singh that the coloring agent is provided in a form and sufficient amount to cause coloration of a part of the oral and/or pharyngeal cavity such that it is used as a marker to determine whether a patient has complied with a medication regimen, as is recited in the claims of the present application. As described above with respect to the rejection under 35 U.S.C. § 102, the amount of coloring agent in the Singh composition, while providing color to the tablet, does not provide an amount sufficient to cause significant coloring such that it is visually observable after ingestion to determine compliance, and other issues, such as the duration since the last medication. In Singh, the amount of

coloring agent in the composition is recited in the Examples as between .005 and .030 weight percent of the total composition. Applicants assert that this is not a sufficient amount to cause an observable coloration in a patient in order to determine compliance. Any instantaneous, minor coloring presented immediately after the prior art composition is consumed would be so short-lasting or fleeting that to even be possibly observed, it would have to be done so immediately. That is, the observer might as well be present to dispense the medication. As may be appreciated, this defeats the entire purpose of the invention. Singh does not disclose a marker in an amount to observe to determine compliance.

Nor does Pather disclose a marker in an amount sufficient to cause contact coloration in an oral and/or pharyngeal membrane to be observed to determine compliance with a medication regimen. Pather is directed to a sublingual buccal effervescent. Applicants note that while Pather does list various coloring agents, including carmine, in an oral composition, such coloring agents find their use solely for the purpose of imparting a particular color to the composition of Pather. They have no purpose and indeed teach no purpose beyond that. In other words, like the coloring agents of Singh and Blase, the coloring agents of Pather are used to provide an aesthetic, cosmetic characteristic (color) to the composition, much like a flavoring agent would be used to make the composition more palatable. There is no teaching in Pather that such coloring agents function as anything but as a superficial component for

aesthetic and cosmetic purposes. Again, these are essentially "throw-away" components with respect to the therapeutic action provided by the composition. They certainly do not teach the invention utilizing a marker in a form and sufficient amount to cause coloration of a patient cavity for subsequent visual observation.

Applicants submit that the use of coloring agents as "throw-away" components in Pather is very apparent when one considers the disclosure of column 5, lines 1-6 when taken in view of the paragraph at column 4, lines 52-58 of Pather. The paragraph concerning coloring at column 5, lines 1-6 is introduced earlier in the paragraph of column 4, lines 52-58 as a mere list of ingredients which may be included in the composition. These ingredients may include "glidants, lubricants, binders, sweetener, flavoring, and coloring components." The subsequent paragraphs go on to simply list examples of these coloring ingredients. However, there is no indication that the coloring agent plays any significant role in the composition of Pather, nor does Pather teach that the coloring agent is present in a form and amount sufficient to stain the oral and/or pharyngeal cavity for subsequent visual observation to determine compliance with a medication regimen. In contrast, the coloring agent of the composition of the present application is what allows an observer to determine compliance, duration since last medication, remaining time until next medication, etc. There simply is no teaching in Pather by which one of skill in the art may use the composition disclosed therein to obtain such information.

Further, as mentioned above, Applicants assert that there is absolutely no teaching in Pather that the coloring agent is provided in a form and sufficient amount to cause coloration of a part of the oral and/or pharyngeal cavity such that it is used as a marker to determine whether a patient has complied with a medication regimen, as is recited in the claims of the present application. First, the composition of Pather is taught as having a wholly different purpose than that of the present application. Reference to the entirety of Pather makes it quite clear that the purpose of the composition of that reference lies in that it includes an effervescent to promote absorption of the medicament directly into the oral cavity. Nowhere does Pather discuss or teach that the use of the coloring agent is part of a method for monitoring patient compliance. Rather, as described above, the coloring agent of Pather is merely used to impart an aesthetic, cosmetic quality to the composition. Second, the amount of coloring agent in the prior art composition, while providing color to the tablet, does not provide an amount sufficient to cause significant coloring such that it is visually observable after ingestion to determine compliance, and other issues, such as the duration since the last medication. In Pather, the amount of coloring agent in the composition is recited at col. 5 as 0.1 - 3.5 weight percent of the total composition. Applicants assert that this is not a sufficient amount to cause an observable coloration in a patient in order to determine compliance. Any instantaneous, minor coloring presented immediately after the prior art composition is consumed would be so short-

lasting or fleeting that to even be possibly observed, it would have to be done so immediately. That is, the observer might as well be present to dispense the medication. Like Singh and Blase, as may be appreciated, this defeats the entire purpose of the invention.

Therefore, neither Singh nor Pather discloses a marker provided in a sufficient amount and form to cause a contact coloration of at least a portion of the oral and/or pharyngeal cavity for determining whether a patient is in compliance with a medication regimen. Thus, any combination of Singh and Pather does not disclose this limitation of claim 15, which is incorporated in claim 21. As a result, claim 21 cannot be rendered obvious by the combination of Singh and Pather. Further, since Singh and Pather (and the colorants thereof) are directed to different compounds with different uses for different purposes, there would be no motivation for one skilled in the art to combine the two references. Applicants thus respectfully request a withdrawal of the rejection of claim 21.

4. **Singh/Blase**

The Examiner has rejected claims 23 and 25-27 under 35 U.S.C. § 103(a) as unpatentable over Singh in view of Blase. In particular, the Examiner states that Singh does not disclose multiple markers, but that these are disclosed by Blase. Applicants respectfully disagree.

Claims 23 and 25-27 each ultimately depend from claim 15 and thus incorporate the limitations of claim 15. As described above, claim 15 is not anticipated by Singh. Thus, for claims 23 and 25-27 to be rendered obvious by the combination of Singh and Blase, claim 15 must either (1) be anticipated by Blase, or (2) be obvious in view of Singh and Blase. However, Applicants assert that neither Singh nor Blase teaches a coloring agent provided in an amount to cause coloration of the oral and/or pharyngeal cavity to determine compliance with a medication regimen. Thus, neither Singh nor Blase, alone or in combination, can anticipate or render obvious claim 15. And thus, the combination of Singh and Blase cannot render claims 23 and 25-27 obvious.

As described above, Applicants assert that there is absolutely no teaching in Singh that the coloring agent is provided in a form and sufficient amount to cause coloration of a part of the oral and/or pharyngeal cavity such that it is used as a marker to determine whether a patient has complied with a medication regimen, as is recited in the claims of the present application. In particular, the amount of coloring agent in the prior art composition, while providing color to the tablet, does not provide an amount sufficient to cause significant coloring such that it is visually observable after ingestion to determine compliance, and other issues, such as the duration since the last medication. In Singh, the amount of coloring agent in the composition is recited in the Examples as between .005 and .030 weight percent of the total composition.

Applicants assert that this is not a sufficient amount to cause an observable coloration in a patient in order to determine compliance. Any instantaneous, minor coloring presented immediately after the prior art composition is consumed would be so short-lasting or fleeting that to even be possibly observed, it would have to be done so immediately. That is, the observer might as well be present to dispense the medication. As may be appreciated, this defeats the entire purpose of the invention.

Applicants further submit that Blase does not cure the defects of Singh, because Blase does not provide any of the elements of claim 15 that are missing from Singh. Blase does not teach contact coloration to be observed to determine compliance. In Blase, the amount of coloring agent in the composition is recited in Table 1 and in the Example as between .0005 and .003 g per 100 ml of the composition. Applicants assert that this is not a sufficient amount to cause an observable coloration in a patient in order to determine compliance. Any instantaneous, minor coloring presented immediately after the Blase composition is consumed would be so short-lasting or fleeting that to even be possibly observed, it would have to be done so immediately. That is, the observer might as well be present to dispense the medication. As may be appreciated, this defeats the entire purpose of the invention.

Also, the Examiner cites Blase for its disclosure of multiple dyes (being multiple markers). Applicants disagree. The purpose of using multiple dyes in one

composition in Blase is to mix two colors to produce a third color for the suspension (see column 10, lines 6-9, discussing the mixing of blue and red coloring agents to provide a purple color to the composition). This in no way discloses multiple markers as described in the present application (for example, see p. 17, lines 6-16 of the application, disclosing a composition including a first marker detectable under natural light and a second marker detectable only under light that causes fluorescence, wherein each marker has a different duration).

Thus, neither Singh nor Blase discloses a marker provided in a sufficient amount and form to cause a contact coloration of at least a portion of the oral and/or pharyngeal cavity for determining whether a patient is in compliance with a medication regimen. Thus, any combination of Singh and Blase does not disclose this limitation of claim 15, which is incorporated in claims 23 and 25-27. Thus, claims 23 and 25-27 cannot be rendered obvious by the combination of Singh and Blase. Further, neither of the references teaches multiple markers as disclosed in the present application. Further, since Singh and Blase (and the colorants thereof) are directed to different compounds with different uses for different purposes, there would be no motivation for one skilled in the art to combine the two references. Applicants thus respectfully request a withdrawal of the rejection of claims 23 and 25-27.

Conclusion:

For the foregoing reasons, Applicants submit that all claims are patentable and a Notice of Allowance is respectfully requested.

The Commissioner is hereby authorized to charge Deposit Account No. 23-3000 in the amount of $18.00 for two newly added claims. No additional fee is believed due with this submission. However, if any additional fee or surcharges are deemed due, please charge same or credit any overpayment to Deposit Account No. 23-3000.

The Examiner is invited to contact the undersigned attorney with any questions or remaining issues.

Respectfully submitted,

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